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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/829,545	04/10/2001	Richard M. Weinshilbourn	07039-118002	8183

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EXAMINER

PROUTY, REBECCA E

ART UNIT PAPER NUMBER

1652

DATE MAILED: 10/22/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.
09/829,545

Applicant(s)
Weinshilboum et al.

Examiner
Rebecca Prouty

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1652



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on _____.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 14-17 and 32-36 is/are pending in the application.
- 4a) Of the above, claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 14-17 and 32-36 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
*See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 4 6) ☐ Other:

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Claims 1-13 and 18-31 have been canceled. Claims 14-17 and 32-36 are at issue and are present for examination.

Claims 14-17 and 32-36 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 14-17 and 32-36 recite methods for determining a risk estimate of a hormone-dependent disease in a subject by detecting the presence of a sulfotransferase nucleotide sequence variant and making a risk estimate based on the results. The specification and art each disclose that sulfonation of a wide variety of organic compounds with known or suspected connections to a variety of diseases is important to the bioactivity of these compounds, that a number of sulfotransferases are expressed in mammalian cells of which the encoding genes for many have been cloned, and that a number of polymorphisms of some these genes exist. However, the ability to determine the risk of a hormone dependent disease from the presence or absence of a particular polymorphism require a clear knowledge of an established correlation between the presence/absence of a specific allele associated with the site detected and the presence of the disease. Such correlations are very difficult to establish in

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view of the extremely complex nature of the art. A wide variety of factors influence the development of any hormone-dependent disease and the presence of any correlation to a polymorphism of any gene and these factors are not necessarily the same in every hormone-dependent disease nor are each of the factors of similar importance in each individual disease. While sulfotransferases are clearly important enzymes in the bioactivity of many organic compounds, the effects of sulfonation may increase the activity or toxicity of some compounds and decrease the activity or toxicity of others. Sulfonation is a well known part of the degradation/elimination pathways of many potential carcinogens but also known to be important for the activation of other compounds. As such changes in activity of any sulfotransferase might have diverse effects on the development of cancers induced by different carcinogens and might increase the risk of one type of cancer while simultaneously decreasing the risk of another type of cancer. Furthermore, there are a large number of different sulfotransferase genes which are differently expressed in distinct tissue types and have sometimes overlapping and sometimes distinct substrate specificities such that a polymorphism which increased/decreased the activity of one sulfotransferase might have diverse effects on the development of cancer in different tissues depending of whether other

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sulfotransferases catalyzing the same reaction are present or absent in each of those tissues. Not only are there large numbers of different sulfotransferases, the presence/absence of many other enzymes involved in the bioactivation, degradation and/or elimination of any particular compound which can each have multiple different polymorphic forms further complicate the evaluation of the risk of any disease related to a particular compound and the correlation of changes in activity in any one enzyme to changes in the risk for the disease. For a good review of the knowledge of the prior art with regard to the influence of polymorphisms in sulfotransferases in cancer susceptibility see Hengstler et al.

The specification fails to teach that even a single one of the disclosed polymorphisms of the 3 phenol sulfotransferase genes (i.e., SULT1A1, SULT1A2 and SULT1A3) discussed has a defined correlation to any particular hormone dependent disease. In fact the specification fails to disclose even a difference in activity of the encoded sulfotransferase for all but the single polymorphism at nucleotide 638 of SULT1A1 which encodes the SULT1A1*2 allele. However even for this allele there is no showing that the differences in activity of the alleles correlates with an increased or decreased risk for even a single hormone dependent disease much less for any hormone-dependent

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disease. While the skilled artisan might expect that this polymorphism might be correlated with increased/decreased risk for some diseases, it would take undue experimentation to determine how even the presence or absence of any one allele of even this particular polymorphism correlates with such risk as the correlation may be different for distinct diseases as well as for distinct causes of even the same disease and the number of factors involved is immense. Determining a correlation between any other known polymorphism of any of the 3 phenol sulfotransferases would be even worse as there is not even any showing of differences in activity of the encoded enzyme associated with the polymorphism and applicants claims in fact encompass even the use of genes for which they have not disclosed **any** polymorphisms (i.e., they are not limited to phenol sulfotransferase gene polymorphisms) and the assessment of risk for unknown polymorphisms as well. As such it would require undue experimentation for one to determine the risk of any hormone dependent disease by determining the presence or absence of any polymorphism (or even the presence or absence of the SULT1A1*2 allele) of any sulfotransferase gene.

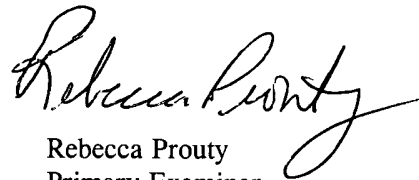
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rebecca Prouty, Ph.D. whose telephone number is (703) 308-4000. The

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examiner can normally be reached on Monday-Friday from 8:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy, can be reached at (703) 308-3804. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

A handwritten signature in cursive script, reading "Rebecca Prouty".

Rebecca Prouty
Primary Examiner
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